

IN THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

Claims 1-58 (cancelled)

Claim 59 (previously presented): A replication-competent adenoviral vector for selective cytotoxicity of a target cell, comprising first and second genes co-transcribed as a single mRNA wherein said first and second genes are under transcriptional control of a heterologous, target cell-specific transcriptional regulatory element (TRE), and wherein said first gene is an adenoviral gene and said second gene has a mutation or a partial deletion of its endogenous promoter and is under translational control of an internal ribosome entry site (IRES).

Claim 60 (previously presented): The adenoviral vector of Claim 59, wherein said first gene is an adenoviral early gene essential for replication selected from the group consisting of E1A, E1B, E2 and E4.

Claim 61 (previously presented): The adenoviral vector of Claim 59, wherein said adenoviral gene is a late gene.

Claim 62 (previously presented): The adenoviral vector of Claim 60, wherein said TRE is selected from the group consisting of a prostate antigen specific TRE (PSA-TRE), a glandular kallikrein TRE (hk-TRE), a probasin TRE (PB-TRE), an alpha-fetoprotein TRE (AFP-TRE), a carcinoembryonic antigen TRE (CEA-TRE), a cell status TRE, a melanocyte cell-specific TRE, a mucin (MUC1) TRE, and a uroplakin TRE (UP-TRE).

Claim 63 (previously presented): The adenoviral vector of Claim 62, wherein said glandular kallikrein TRE is a human glandular kallikrein TRE (hKLK2 TRE).

Claim 64 (previously presented): The adenoviral vector of Claim 62, wherein said cell status TRE is an E2F-1 TRE.

Claim 65 (previously presented): The adenoviral vector of Claim 62, wherein said melanocyte cell-specific TRE is a tyrosinase TRE or a MART-1 TRE.

Claim 66 (previously presented): The adenoviral vector of Claim 62, wherein said uroplakin TRE (UP-TRE) is a human uroplakin II TRE.

Claim 67 (previously presented): The adenoviral vector of Claim 59, wherein said second gene is a therapeutic gene selected from the group consisting of herpes simplex virus thymidine kinase (HSV-tk), a cytosine deaminase (cd) gene, genes encoding the A chain of diphtheria toxin, ricin and abrin, a gene encoding a factor capable of initiating apoptosis, and a cytokine gene.

Claim 68 (previously presented): The adenoviral vector of Claim 67 wherein said therapeutic gene encodes HSV-tk.

Claim 69 (previously presented): The adenoviral vector of Claim 67, wherein said cytokine encoding gene is selected from the group consisting of interleukin-1 (IL 1), IL 2, IL 6, IL 12, granulocyte macrophage colony stimulating factor (GM-CSF), granulocyte colony stimulating factor (G-CSF), macrophage colony stimulating factor (M-CSF), interferon (IFN)-alpha, IFN-beta, IFN-gamma, tumor necrosis factor (TNF)-alpha, TNF-beta, transforming growth factor (TGF)-alpha, TGF-beta and nerve growth factor (NGF).

Claim 70 (previously presented): The adenoviral vector of Claim 69 wherein said cytokine encoding gene is GM CSF.

Claim 71 (previously presented): The adenoviral vector of Claim 67 wherein said gene encoding a factor capable of initiating apoptosis is a Fas gene.

Claim 72 (previously presented): The adenoviral vector of Claim 59 wherein said second gene is a reporter gene.

Claim 73 (previously presented): The adenoviral vector of Claim 72 wherein said reporter gene is selected from the group consisting of lacZ gene, luciferase, alkaline phosphatase and green fluorescent protein.

Claim 74 (currently amended): The adenoviral vector of Claim 60, wherein said first gene has a mutation or a partial deletion of its endogenous promoter.

Claim 75 (previously presented): The adenoviral vector of Claim 60, wherein said first gene has a deletion or inactivation of an enhancer region.

Claim 76 (previously presented): The adenoviral vector of Claim 74, wherein said first gene is an E1A gene and the endogenous E1A promoter is mutated or partially deleted.

Claim 77 (previously presented): The adenoviral vector of Claim 75, wherein said first gene is an E1A gene and the endogenous E1A enhancer I is mutated or partially deleted.

Claim 78 (previously presented): The adenoviral vector of Claim 74, wherein said first gene is an E1B gene and the endogenous E1B promoter is mutated or partially deleted.

Claim 79 (previously presented): The adenoviral vector of Claim 75, wherein said first gene is an E1B gene which has a deletion in or mutation of the 19-kDa region.

Claim 80 (previously presented): The adenoviral vector of Claim 59, wherein said adenoviral vector comprises an E3 region.

Claim 81 (previously presented): The adenoviral vector of Claim 80, wherein said adenoviral vector comprises at least one intact open reading frame from the adenovirus E3 region selected from the group consisting of gp19k protein, 14.7k protein and 10.4k/14.5k protein complex.

Claim 82 (previously presented): The adenoviral vector of Claim 59, wherein said IRES is from encephalomyocarditis virus (EMCV).

Claim 83 (previously presented): The adenoviral vector of Claim 59, wherein said IRES is from vascular endothelial growth factor (VEGF).

Claim 84 (previously presented) A composition comprising an adenoviral vector according to Claim 62, and a pharmaceutically acceptable excipient.

Claim 85 (previously presented): A composition comprising an adenoviral vector according to Claim 70, and a pharmaceutically acceptable excipient.

Claim 86 (previously presented): An isolated host cell comprising an adenoviral vector according to Claim 62.

Claim 87 (previously presented): An isolated host cell comprising an adenoviral vector according to Claim 70.

Claim 88 (withdrawn): A method for propagating a replication-competent adenovirus vector comprising a target cell-specific TRE, said method comprising combining an adenovirus vector of Claim 59 ex vivo with mammalian cells that permit the function of a target cell-specific TRE, such that the adenovirus vector enters the cell and said adenovirus vector is propagated.